Are Certain Category A Biological Agents More Suitable For Bioterrorism Than Others?

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Bioterrorism – Why the Concern?

- Terrorist interest in biological weapons
  - Aum Shinrikyo – Botulinum toxin, anthrax
  - Al Qaeda – Anthrax (speculated)
  - Anthrax attacks of 2001
- Nature of BW
  - Inexpensive
  - Most agents available from environment
  - Fewer technical skills required than some WMD (e.g. nuclear)
  - Difficult to detect BW programs
  - Some diseases are transmissible
  - Agents replicate
- Prevalence of US adversaries
  - Al Qaeda
  - Shining Path
  - Lashkar-e-Tayiba
  - Right-wing domestic groups

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Category A, B, and C Agents

- Agents prioritized by the CDC based on
  - Public health impact
  - Transmission and dispersion characteristics
  - Availability of effective medical countermeasures
  - Special public health preparedness measures needed to address the disease caused by each agent
- Resulting categories
  - A – Greatest potential for adverse public health impact
  - B – Some potential for large scale dissemination but would result in fewer illnesses and deaths than Category A Agents (e.g. Ricin)
  - C – Not currently believed to represent a high risk, but could in the future (e.g. Hantavirus)
- CDC evaluation of agents does not specifically address ease or difficulty of developing agents as *weapons*
  - Availability of agent, ability to culture agent, amount of agent that can be produced, environmental hardiness, etc.
- Hypothesis: An analysis that addresses both "weaponization potential" and consequences could help discriminate the bioterrorism utility among the Category A agents

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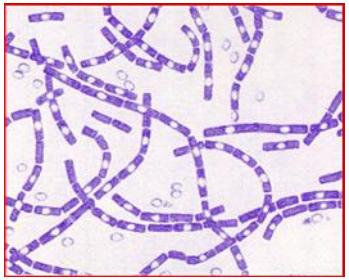
Our Methodology

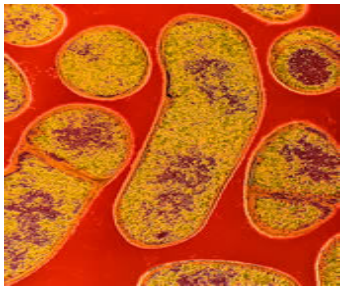
- Category A agents chosen because of the perception that they represent the greatest risk for bioterrorism
- Study based upon a survey of the open literature
  - Not based upon SNL experimental results
- Used criteria for which data was available for all of the agents
  - Inherent variability of pertinent agent information (e.g. availability, infectious dose, transmission rates, etc.)
- Applied a SNL risk analysis framework that allowed for an initial bioterrorism risk assessment of the Category A agents relative to one another
  - Initial and tentative conclusions

The Category A Agents

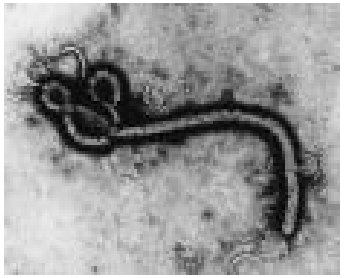
- **Hemorrhagic fever viruses (e.g. Ebola)**
- **Botulinum toxin (*C. botulinum*)**
- ***Bacillus anthracis* (anthrax)**
- ***Francisella tularensis* (tularemia)**
- ***Yersinia pestis* (plague)**
- **Variola major (smallpox)**



Bacillus anthracis



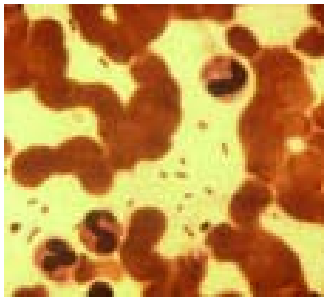
Clostridium botulinum



Ebola virus

Francisella tularensis

Variola major



Yersinia pestis

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Risk Assessment Criteria

- We consider the risk of agent use as a biological weapon to be a function of
  - Weaponization potential
  - Consequences of malicious use

- Weaponization potential
  - Acquisition/procurement (e.g. lab, culture collection)
  - Production (suitable quantity in a suitable form)
  - Dissemination (e.g. aerosol, food, water)

- Consequences of malicious use
  - Morbidity: incidence and severity of disease
  - Mortality rate: number of deaths relative to the total number of infected individuals
  - Availability of medical countermeasures: vaccines, therapeutics

Acquisition

- **Hemorrhagic fever viruses**
  - **Arenaviruses – Natural hosts (rodents), limited number of legitimate facilities**
  - **Filoviruses – Limited number of legitimate facilities, natural reservoir unknown**
- **Botulinum toxin**
  - **Many legitimate facilities, including pharmaceutical and biotech companies**
- ***Bacillus anthracis***
  - **Many legitimate facilities, widely endemic**
- ***Francisella tularensis***
  - **Many legitimate facilities, widely endemic**
- ***Yersinia pestis***
  - **Many legitimate facilities, widely endemic**
- **Variola major**
  - **Only two *known* repositories**

Production

- Hemorrhagic fever viruses
  - Arenaviruses – viral culture, animal hosts
  - Filoviruses – viral culture, animal hosts
- Botulinum toxin
  - Bacterial culture followed by toxin purification
- *Bacillus anthracis*
  - Bacterial culture, spores form upon exposure to air
- *Francisella tularensis*
  - Bacterial culture
- *Yersinia pestis*
  - Bacterial culture
- Variola major
  - Viral culture

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Dissemination: Aerosol Stability

- Aerosol dispersion of agents assumed to cause the highest consequences
  - Affected by U.V. radiation, oxidation, heat, etc.
- Hemorrhagic fever viruses
  - Moderate aerosol stability (hours)
- Botulinum toxin
  - Proteins not generally stable as aerosols
- *Bacillus anthracis*
  - Highest aerosol stability (days) for Category A agents
  - Electrostatic attraction a possible complication
- *Francisella tularensis*
  - Moderate aerosol stability (hours)
- *Yersinia pestis*
  - Low natural aerosol stability
  - Methods exist to increase to moderate stability (hours)
- Variola major
  - High aerosol stability (~day)

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Morbidity

- **Viral Hemorrhagic Fevers**
  - **Arenaviruses – Fever, prostration, hemorrhage**
  - **Filoviruses – Fever, prostration, severe hemorrhage**
- **Botulism**
  - **Paralysis, possibly months for recovery**
- **Anthrax**
  - **Severe flu-like symptoms, weeks in hospital for recovery**
- **Tularemia**
  - **Severe flu-like symptoms, including acute fever, chills, headache, prolonged recovery**
- **Plague (pneumonic)**
  - **Severe flu-like symptoms (pneumonic plague)**
- **Smallpox**
  - **Acute fever, severe prostration, headache, backache, rash, and pustules**

Patient's leg covered in smallpox

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Mortality Rate (Unvaccinated/Untreated)

- **Viral Hemorrhagic fevers**
  - **Arenaviruses – 3-30%**
  - **Filoviruses – Ebola 50-90%, Marburg 23%**
- **Botulism**
  - **Relatively high, depends on dose (LD_{50} inhalation: 70 µg/person)**
- **Anthrax**
  - **80% (inhalational)**
- **Tularemia**
  - **30-60% (inhalational)**
- **Plague (pneumonic)**
  - **95-100% (inhalational/pneumonic plague)**
- **Smallpox**
  - **30%**

Medical Countermeasures

- **Viral Hemorrhagic Fevers**
  - **Arenaviruses – Antibodies, antivirals (IND protocol), barrier precautions, isolation (transmissible)**
  - **Filoviruses – Supportive care, barrier precautions, isolation (transmissible), no effective therapeutics or prophylactic**
- **Botulism**
  - **Pre-exposure vaccination – Available, but not recommended for general public (side effects)**
  - **Antitoxin – Must be given before onset of symptoms to prevent paralysis (12-72 hours)**
  - **Artificial respiration – Generally prevents death, not symptoms**
- **Anthrax**
  - **Pre-exposure vaccination – Available, not recommended for general public (side effects)**
  - **Antibiotics – 60 day regimen, prompt administration critical**

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Medical Countermeasures (cont.)

- **Tularemia**
  - **Antibiotics – Prompt administration necessary**
- **Plague (pneumonic)**
  - **Antibiotics – Prompt administration critical**
  - **Isolation – Transmissible (pneumonic plague)**

- **Smallpox**
  - **Vaccine – Pre and post-exposure; pre-exposure not recommended for general public (side effects), post-exposure time dependent (days)**
  - **Isolation – Transmissible**

- **Medical countermeasures summary**
  - **No cures or prophylaxis for Filovirus infections**
  - **Diseases caused by other Category A agents are treatable**
  - **Prompt and effective administration of treatment could be difficult**

Criteria That Most Differentiate The Category A Agents

- Acquisition
  - Must acquire the agent to use it
  - e.g. Variola major vs. botulinum toxin
- Mortality rate
  - Death is assumed to be the highest consequence
  - e.g. Smallpox vs. pneumonic plague

- Remaining assessment criteria have similar results or lack sufficient data
  - Production
  - Dissemination
  - Morbidity
  - Availability of medical countermeasures
  - What about transmissibility?

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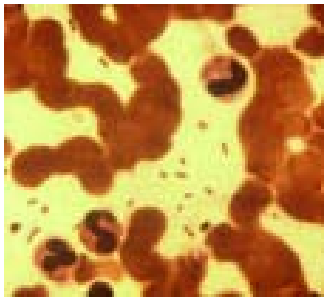
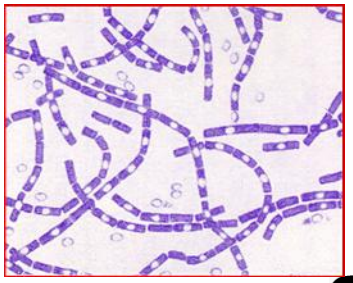
Relative Risk
(based on only two criteria)

- **Variola major**
  - **Acquisition - Extremely difficult**
  - **Mortality rate - Moderate**
  - **Risk - Low**
- **Hemorrhagic fever viruses**
  - **Acquisition - Difficult**
  - **Mortality rate - Moderate to high**
  - **Risk - Low**
- **Botulinum toxin**
  - **Acquisition - Relatively easy**
  - **Mortality rate - Moderate (dose dependent)**
  - **Risk - Moderate**
- ***Francisella tularensis***
  - **Acquisition - Relatively easy**
  - **Mortality rate - Moderate**
  - **Risk – Moderate**
- ***Yersinia pestis***
  - **Acquisition - Relatively easy**
  - **Mortality rate - High**
  - **Risk – High**
- ***Bacillus anthracis***
  - **Acquisition - Relatively easy**
  - **Mortality rate - High**
  - **Risk - High**



Yersinia pestis



Bacillus anthracis

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Relative Risk
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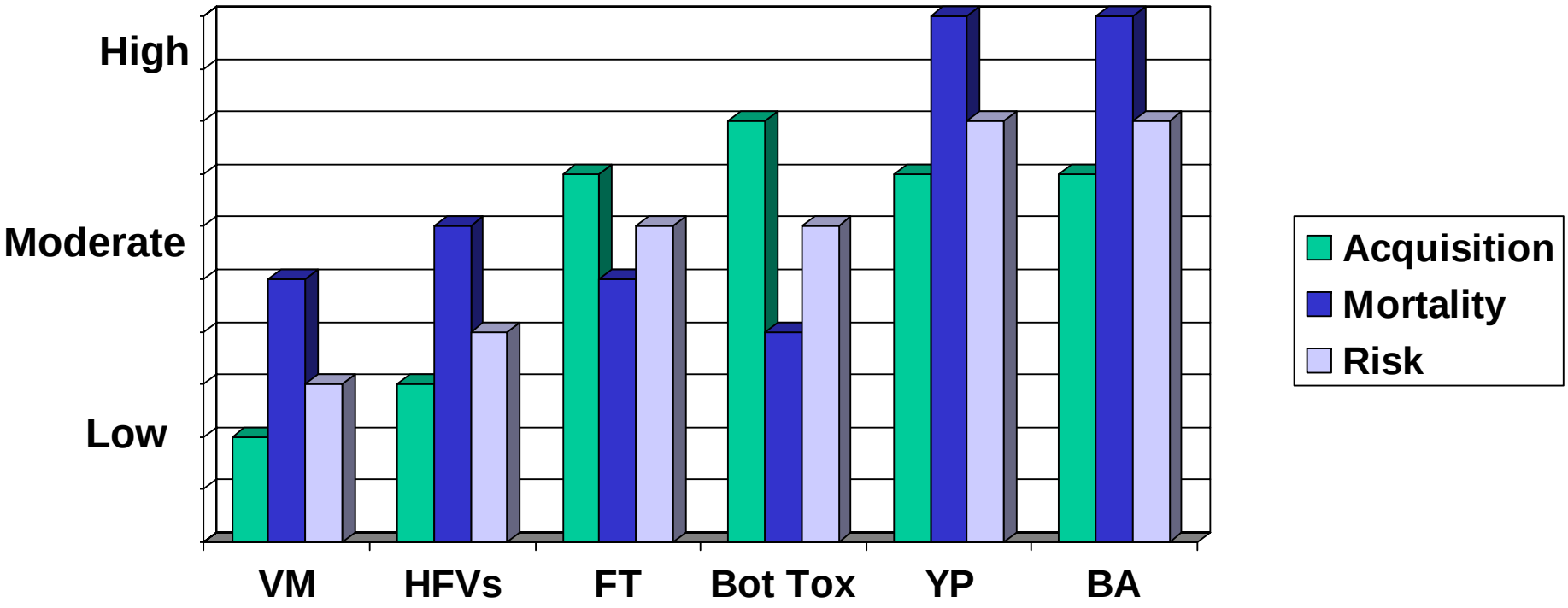

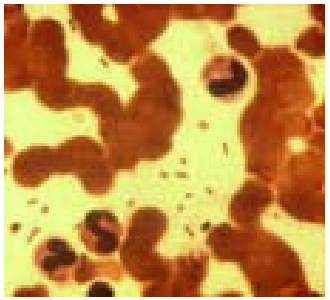

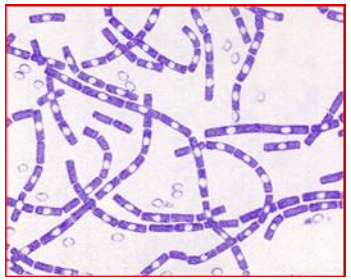

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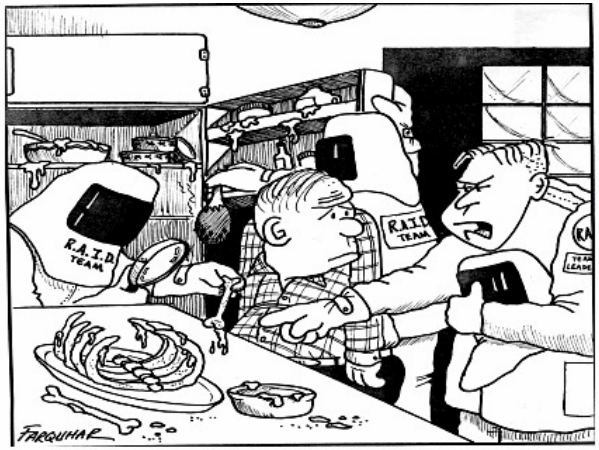
Summary

- Not a definitive study of all biological agents or even all characteristics associated with Category A agents
- Risk assessment is necessary to distinguish among the wide variety of biological agents and their utility for bioterrorism
- US and international bioterrorism prevention and response technologies, policies, and allocation of resources should be based on a comprehensive biological agent risk assessment process



"NO SIR, YOUR HOLIDAY LEFTOVERS DO NOT QUALIFY AS A BIOLOGICAL THREAT! "

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Questions/Discussion

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